09/865950

d his

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L2         1252 S E1-E31
                S L2 AND C18 H23 F2 N O3/MF

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L3           20 S C18 H23 F2 N O3/MF

     FILE 'CAPLUS' ENTERED AT 16:55:25 ON 01 JUL 2003
L4           12 S L3
L5            2 S L2 AND L4

     FILE 'REGISTRY' ENTERED AT 16:56:30 ON 01 JUL 2003
L6           31 S L2
L7            1 S L6 AND  C16 H19 F2 N O2/MF
L8            1 S L7
L9            1 S L6 AND C18 H23 F2 N O3/MF

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=> s l6 and  C16 H19 F2 N O2/mf
            14 C16 H19 F2 N O2/MF
L7           1 L6 AND  C16 H19 F2 N O2/MF

=> d scan

L7   1 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-oxo-1-phenylpropyl]- (9CI)
MF   C16 H19 F2 N O2

Absolute stereochemistry.
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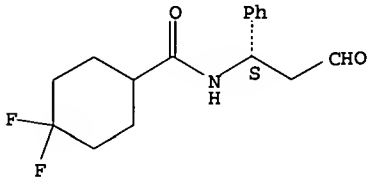


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


ALL ANSWERS HAVE BEEN SCANNED


=> s l7
            14 C16 H19 F2 N O2/MF
L8           1 L6 AND  C16 H19 F2 N O2/MF

=> d all

L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   376348-78-6  REGISTRY
CN   Cyclohexanecarboxamide, 4,4-difluoro-N-[(1S)-3-oxo-1-phenylpropyl]- (9CI)
     (CA INDEX NAME)
FS   STEREOSEARCH
MF   C16 H19 F2 N O2
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Ring System Data
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Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
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C6	C6	6	C6	46.150.18	1

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Absolute stereochemistry.
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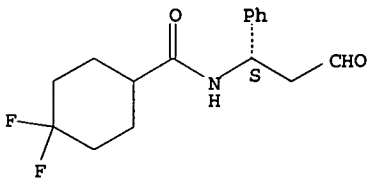


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Calculated Properties (CALC)
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PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	16.0	pH 1	(1) ACD
Bioconc. Factor (BCF)	16.1	pH 4	(1) ACD
Bioconc. Factor (BCF)	16.1	pH 7	(1) ACD
Bioconc. Factor (BCF)	16.1	pH 8	(1) ACD

Bioconc. Factor (BCF)	16.1	pH 10	(1) ACD
Boiling Point (BP)	461.4+/-40.0 deg C	760.0 Torr	(1) ACD
Enthalpy of Vap. (HVAP)	72.23+/-3.0 kJ/mol		(1) ACD
Flash Point (FP)	232.9+/-49.2 deg C		(1) ACD
Freely Rotatable Bonds (FRB)	6		(1) ACD
H acceptors (HAC)	3		(1) ACD
H donors (HD)	1		(1) ACD
Koc (KOC)	253	pH 1	(1) ACD
Koc (KOC)	254	pH 4	(1) ACD
Koc (KOC)	254	pH 7	(1) ACD
Koc (KOC)	254	pH 8	(1) ACD
Koc (KOC)	254	pH 10	(1) ACD
logD (LOGD)	1.89	pH 1	(1) ACD
logD (LOGD)	1.89	pH 4	(1) ACD
logD (LOGD)	1.89	pH 7	(1) ACD
logD (LOGD)	1.89	pH 8	(1) ACD
logD (LOGD)	1.89	pH 10	(1) ACD
logP (LOGP)	1.891+/-0.582		(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 1	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 4	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 7	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 8	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 10	(1) ACD
Molecular Weight (MW)	295.32		(1) ACD
Vapor Pressure (VP)	1.07E-08 Torr	25.0 deg C	(1) ACD

(1) Calculated using Advanced Chemistry Development (ACD) Software Solaris V4.76 ((C) 1994-2003 ACD)

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 136:6195 CA
TI Preparation of therapeutic tropane derivatives
IN Perros, Manoussos; Price, David Anthony; Stammen, Blanda Luzia Christa; Wood, Anthony
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D451-00
CC 31-3 (Alkaloids)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090106	A2	20011129	WO 2001-IB806	20010509
	WO 2001090106	A3	20020328		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1284974	A2	20030226	EP 2001-925808	20010509
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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	US 2002013337	A1	20020131	US 2001-865950	20010525
	NO 2002005227	A	20021031	NO 2002-5227	20021031
PRAI	GB 2000-14046	20000526			
	GB 2000-15835	20000627			
	US 2000-214587P	20000627			
	US 2000-219202P	20000719			
	WO 2001-IB806	20010509			

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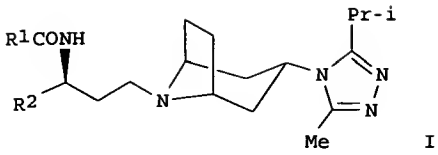

I

AB The tropanes I (R1 = C3-6 cycloalkyl optionally substituted by one or more fluorine atoms, C1-6 alkyl optionally substituted by one or more fluorine atoms, C3-6 cycloalkylmethyl optionally ring-substituted by one or more fluorine atoms; R2 = Ph optionally substituted by one or more fluorine atoms) and their pharmaceutically acceptable salts and solvates were prepd. Thus, (1S)-3-[3-(3-isopropyl-5-methyl-4H-1,2,4-triazol-4-yl)-exo-8-azabicyclo[3.2.1]oct-8-yl]-1-phenyl-1-propanamine, prepn. given, was treated with cyclobutanecarboxylic acid in presence of polymer bound N-benzyl-N'-cyclohexylcarbodiimide to give I (R1 = cyclobutyl, R2 = Ph). I had an IC50 value of less than 10nM in the assay for CCR5 binding.

ST tropane deriv prepn CCR5 receptor

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CCR5; prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Intestine, disease
(inflammatory; prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Anti-AIDS agents
Anti-inflammatory agents
Crystal structure
Molecular structure
Respiratory distress syndrome
Respiratory tract, disease
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 376348-65-1P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 376348-62-8P 376348-63-9P 376348-64-0P 376348-66-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 696-59-3, 2,5-Dimethoxytetrahydrofuran 3082-69-7 3287-99-8, Benzylamine hydrochloride 120686-18-2 122665-97-8 376348-71-9 376348-74-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 28957-72-4P 37088-66-7P 76272-34-9P 76272-36-1P 135865-78-0P 190189-97-0P 376348-67-3P 376348-68-4P 376348-69-5P 376348-70-8P 376348-72-0P 376348-73-1P 376348-75-3P 376348-76-4P 376348-77-5P 376348-78-6P 376348-79-7P 376348-80-0P 376348-81-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

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            20 C18 H23 F2 N O3/MF
L9           1 L6 AND C18 H23 F2 N O3/MF

=> d scan

L9   1 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   Benzenepropanoic acid, .beta.-[[(4,4-difluorocyclohexyl)carbonyl]amino]-,
     ethyl ester, (.beta.S)- (9CI)
MF   C18 H23 F2 N O3

Absolute stereochemistry.
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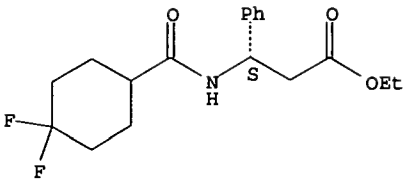


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

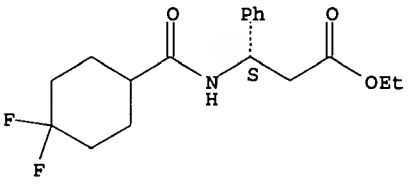
=> d all

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **376348-76-4** REGISTRY
CN Benzenepropanoic acid, .beta.-[[(4,4-difluorocyclohexyl)carbonyl]amino]-, ethyl ester, (.beta.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H23 F2 N O3**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.1	1
C6	C6	6	C6	46.150.18	1

Absolute stereochemistry.



Calculated Properties (CALC)

PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	59.9	pH 1	(1) ACD
Bioconc. Factor (BCF)	60.3	pH 4	(1) ACD
Bioconc. Factor (BCF)	60.3	pH 7	(1) ACD
Bioconc. Factor (BCF)	60.3	pH 8	(1) ACD
Bioconc. Factor (BCF)	60.3	pH 10	(1) ACD
Boiling Point (BP)	500.8+/-50.0 deg C	760.0 Torr	(1) ACD
Enthalpy of Vap. (HVAP)	76.95+/-3.0 kJ/mol		(1) ACD
Flash Point (FP)	256.7+/-54.2 deg C		(1) ACD
Freely Rotatable Bonds (FRB)	8		(1) ACD
H acceptors (HAC)	4		(1) ACD
H donors (HD)	1		(1) ACD
Koc (KOC)	650	pH 1	(1) ACD
Koc (KOC)	654	pH 4	(1) ACD
Koc (KOC)	654	pH 7	(1) ACD
Koc (KOC)	654	pH 8	(1) ACD
Koc (KOC)	654	pH 10	(1) ACD
logD (LOGD)	2.64	pH 1	(1) ACD
logD (LOGD)	2.64	pH 4	(1) ACD
logD (LOGD)	2.64	pH 7	(1) ACD
logD (LOGD)	2.64	pH 8	(1) ACD

logD (LOGD)	2.64	pH 10	(1) ACD
logP (LOGP)	2.645+/-0.570		(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 1	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 4	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 7	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 8	(1) ACD
Molar Solubility (SLB.MOL)	<0.01 mol/L	pH 10	(1) ACD
Molecular Weight (MW)	339.38		(1) ACD
Vapor Pressure (VP)	3.68E-10 Torr	25.0 deg C	(1) ACD

(1) Calculated using Advanced Chemistry Development (ACD) Software Solaris V4.76 ((C) 1994-2003 ACD)

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1

AN 136:6195 CA
TI Preparation of therapeutic tropane derivatives
IN Perros, Manoussos; Price, David Anthony; Stammen, Blanda Luzia Christa; Wood, Anthony
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D451-00
CC 31-3 (Alkaloids)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090106	A2	20011129	WO 2001-IB806	20010509
	WO 2001090106	A3	20020328		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1284974	A2	20030226	EP 2001-925808	20010509
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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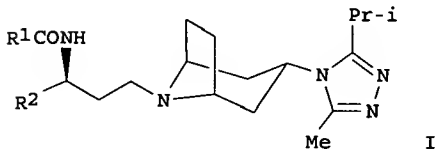
	US 2002013337	A1	20020131	US 2001-865950	20010525
	NO 2002005227	A	20021031	NO 2002-5227	20021031
PRAI	GB 2000-14046	20000526			
	GB 2000-15835	20000627			
	US 2000-214587P	20000627			
	US 2000-219202P	20000719			
	WO 2001-IB806	20010509			

GI



I

AB The tropanes I (R1 = C3-6 cycloalkyl optionally substituted by one or more fluorine atoms, C1-6 alkyl optionally substituted by one or more fluorine atoms, C3-6 cycloalkylmethyl optionally ring-substituted by one or more fluorine atoms; R2 = Ph optionally substituted by one or more fluorine atoms) and their pharmaceutically acceptable salts and solvates were prepd. Thus, (1S)-3-[3-(3-isopropyl-5-methyl-4H-1,2,4-triazol-4-yl)-exo-8-azabicyclo[3.2.1]oct-8-yl]-1-phenyl-1-propanamine, prepn. given, was treated with cyclobutanecarboxylic acid in presence of polymer bound N-benzyl-N'-cyclohexylcarbodiimide to give I (R1 = cyclobutyl, R2 = Ph). I had an IC50 value of less than 10nM in the assay for CCR5 binding.

ST tropane deriv prepn CCR5 receptor

IT Chemokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CCR5; prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Intestine, disease
(inflammatory; prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Anti-AIDS agents
Anti-inflammatory agents
Crystal structure
Molecular structure
Respiratory distress syndrome
Respiratory tract, disease
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT Chemokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 376348-65-1P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 376348-62-8P 376348-63-9P 376348-64-0P 376348-66-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 696-59-3, 2,5-Dimethoxytetrahydrofuran 3082-69-7 3287-99-8, Benzylamine hydrochloride 120686-18-2 122665-97-8 376348-71-9 376348-74-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

IT 28957-72-4P 37088-66-7P 76272-34-9P 76272-36-1P 135865-78-0P 190189-97-0P 376348-67-3P 376348-68-4P 376348-69-5P 376348-70-8P 376348-72-0P 376348-73-1P 376348-75-3P 376348-76-4P 376348-77-5P 376348-78-6P 376348-79-7P 376348-80-0P 376348-81-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of tropane derivs. as CCR5 receptor antagonists)

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L1               1 S E3
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               S L2 AND C18 H23 F2 N O3/MF

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L3              20 S C18 H23 F2 N O3/MF

     FILE 'CAPLUS' ENTERED AT 16:55:25 ON 01 JUL 2003
L4              12 S L3
L5               2 S L2 AND L4

     FILE 'REGISTRY' ENTERED AT 16:56:30 ON 01 JUL 2003
L6              31 S L2
L7               1 S L6 AND  C16 H19 F2 N O2/MF
L8               1 S L7
L9               1 S L6 AND C18 H23 F2 N O3/MF

=> s l9
             20 C18 H23 F2 N O3/MF
L10           1 L6 AND C18 H23 F2 N O3/MF

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L10  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   376348-76-4  REGISTRY
CN   Benzenepropanoic acid, .beta.-[[(4,4-difluorocyclohexyl)carbonyl]amino]-,
     ethyl ester, (.beta.S)- (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C18 H23 F2 N O3
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

Absolute stereochemistry.
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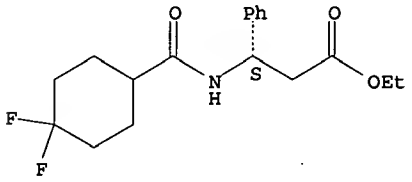


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               1 REFERENCES IN FILE CA (1957 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
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